

WHAT IS CLAIMED IS:

1. A method of lowering intraocular pressure, the method comprising:
 - (a) diagnosing a subject for a condition mediated by elevated intraocular pressure; and
 - (b) administering to the subject an aquaporin modulating agent and an aqueous humor modulating agent, wherein the aqueous humor modulating agent lowers intraocular pressure by a pathway other than the modulation of aquaporin.
2. The method of claim 1 wherein the aquaporin modulating agent is an angiotensin converting enzyme inhibitor.
3. The method of claim 2 wherein the angiotensin converting enzyme inhibitor is selected from the group consisting of enalapril, benazepril, captopril, fosinopril, lisinopril, moexipril, quinapril, ramipril, and trandolapril.
4. The method of 1 wherein the aquaporin modulating agent is a protein kinase C activator.
5. The method of claim 4 wherein the protein kinase C activator is a diacylglycerol mimic.
6. The method of claim 5 wherein the diacylglycerol mimic is a phorbol ester.
7. The method of claim 6 wherein the phorbol ester is selected from the group consisting of phorbol 12, 13 dibutyrate, phorbol 12-myristate-12-acetate, phorbol 12-O-tetradecanoylphorbol 13-acetate, phorbol 12, 13 didecanoate and tetradecanoylphorbol acetate.
8. The method of claim 4 wherein the protein kinase C activator is ionomycin.
9. The method of claim 1 wherein the aquaporin modulating agent is a protein kinase A inhibitor.

10. The method of claim 9 wherein the protein kinase A inhibitor is selected from the group consisting of (5-isoquinolinesulfonyl)piperazine; 1-(5-Isoquinolinesulfonyl)-2-methylpiperazine, 4-cyano-3-methylisoquinoline; adenosine 3',5'-cyclic monophosphorothioate, 2'-O-monobutyryl; adenosine 3',5'-cyclic monophosphorothioate; 8-bromo-2'-monobutyryl, adenosine 3',5'-cyclic monophosphorothioate; 8-piperidino, N-(2-aminoethyl)-5-chloronaphthalene-1-sulfonamide; N-(2-aminoethyl)-5-isoquinolinesulfonamide; N-[2-((p-bromocinnamyl)amino)ethyl]-5-isoquinolinesulfonamide; N-(2-guanidinoethyl)-5-isoquinolinesulfonamide; 4,4',5,5',6,6'-hexahydroxydiphenic acid 2,6,2',6'-dilactone; (5-isoquinolinesulfonyl) homopiperazine; N-[2-(methylamino)ethyl]-5-isoquinolinesulfonamide; and *trans*-3,3',4,5'-tetrahydroxystilbene.

11. The method of claim 1 wherein the aquaporin modulating agent is a vasoactive peptide.

12. The method of claim 11 wherein the vasoactive peptide is a vasopressin.

13. The method of claim 12 wherein the vasopressin is arginine vasopressin.

14. The method of claim 11 wherein the vasoactive peptide is atrial natriuretic peptide or brain natriuretic peptide.

15. The method of claim 1 wherein the aquaporin modulating agent is tetraethylammonium.

16. The method of claim 1 wherein the aquaporin modulating agent is colchicine.

17. The method of claim 1 wherein the aquaporin modulating agent is a vinca alkaloid.

18. The method of claim 1 wherein the aquaporin modulating agent is rhizoxin.

19. The method of claim 1 wherein the aquaporin modulating agent is estramustine.

20. The method of claim 1 wherein the aquaporin modulating agent is nocodazole.
21. The method of claim 1 wherein the aquaporin modulating agent is erbuluzole.
22. The method of claim 1 wherein the aquaporin modulating agent is tubulozole.
23. The method of claim 1 wherein the aqueous humor modulating agent is a prostaglandin or a prostaglandin analog.
24. The method of claim 23 wherein the aqueous humor modulating agent is a prostaglandin.
25. The method of claim 24 wherein the prostaglandin is selected from prostaglandin A, prostaglandin B, prostaglandin D, prostaglandin E, and prostaglandin F.
26. The method of claim 23 wherein the aqueous humor modulating agent is a prostaglandin analog.
27. The method of claim 26 wherein the prostaglandin analog is a prostaglandin FP receptor antagonist.
28. The method of claim 26 wherein the prostaglandin analog is selected from the group consisting of latanaprost, bimatoprost, unoprostone, and travoprost.
29. The method of claim 1 wherein the aqueous humor modulating agent is a beta adrenergic antagonist.
30. The method of claim 29 wherein the beta adrenergic antagonist is selected from the group consisting of betaxolol, carteolol, levobunolol, metipranolol, timolol, and levobetaxolol.

31. The method of claim 1 wherein the aqueous humor modulating agent is an adrenergic agonist.

32. The method of claim 31 wherein the adrenergic agonist is epinephrine or dipivefrin.

33. The method of claim 1 wherein the aqueous humor modulating agent is a cholinergic agonist.

34. The method of claim 33 wherein the cholinergic agonist is selected from the group consisting of pilocarpine, pilocarpine hydrochloride, carbachol, demacarium, echothiophate iodine, and physostigmine.

35. The method of claim 1 wherein the aqueous humor modulating agent is a carbonic anhydrase inhibitor.

36. The method of claim 35 wherein the carbonic anhydrase inhibitor is selected from the group consisting of acetazolamide, methazolamide, dorzolamide hydrochloride ophthalmic solution, dorzolamide hydrochloride-timolol maleate ophthalmic solution, brinzolamide hydrochloride, dorzolamide, and brinzolamide.

37. The method of claim 1 wherein the aquaporin modulating agent is selected from the group consisting of an angiotensin converting enzyme inhibitor, a protein kinase C activator, a protein kinase A inhibitor, a vasoactive peptide, and a vinca alkaloid.

38. The method of claim 37 wherein the aqueous humor modulating agent is selected from the group consisting of a prostaglandin, a prostaglandin analog, a beta adrenergic antagonist, an adrenergic agonist, a cholinergic agonist and a carbonic anhydrase inhibitor.

39. The method of claim 1 wherein the aquaporin modulating agent is selected from the group consisting of enalapril, benazepril, captopril, fosinopril, lisinopril, moexipril, quinapril, ramipril, trandolapril, phorbol 12, 13 dibutyrate, phorbol 12-

myristate-12-acetate, phorbol 12-O-tetradecanoylphorbol 13-acetate, phorbol 12, 13 didecanoate, tetradecanoylphorbol acetate, ionomycin, arginine vasopressin, atrial natriuretic peptide, brain natriuretic peptide, tetraethylammonium, colchicine, rhizoxin, estramustine, nocodazole, erbuluzole, and tubulozole.

40. The method of claim 39 wherein the aqueous humor modulating agent is selected from the group consisting of prostaglandin A, prostaglandin B, prostaglandin D, prostaglandin E, prostaglandin F, latanaprost, bimatoprost, unoprostone, travoprost, betaxolol, carteolol, levobunolol, metipranolol, timolol, levobetaxolol, epinephrine, dipivefrin, pilocarpine, pilocarpine hydrochloride, carbachol, demacarium, echothiophate iodine, physostigmine, acetazolamide, methazolamide, dorzolamide hydrochloride ophthalmic solution, dorzolamide hydrochloride-timolol maleate ophthalmic solution, brinzolamide hydrochloride, dorzolamide, and brinzolamide.

41. A method of treating an ophthalmic disorder in a subject, the method comprising:

- (a) diagnosing a subject in need of treatment for an ophthalmic disorder; and
- (b) administering to the subject an aquaporin modulating agent and an aqueous humor modulating agent, wherein the aqueous humor modulating agent lowers intraocular pressure by a pathway other than the modulation of aquaporin.

42. The method of claim 41 wherein the ophthalmic disorder is selected from the group consisting of idiopathic macular edema, corneal edema, diabetic macular edema, post-cataract macular edema, central serous retinopathy, venous occlusive diseases of the retina, a glaucoma disorder and ocular hypertension.

43. The method of claim 41 wherein the aquaporin modulating agent is selected from the group consisting of an angiotensin converting enzyme inhibitor, a protein kinase C activator, a protein kinase A inhibitor, a vasoactive peptide, and a vinca alkaloid.

44. The method of claim 43 wherein the aqueous humor modulating agent is selected from the group consisting of a prostaglandin, a prostaglandin analog, a beta adrenergic antagonist, an adrenergic agonist, a cholinergic agonist and a carbonic anhydrase inhibitor.

45. The method of claim 41 wherein the aquaporin modulating agent is selected from the group consisting of enalapril, benazepril, captopril, fosinopril, lisinopril, moexipril, quinapril, ramipril, trandolapril, phorbol 12, 13 dibutyrate, phorbol 12-myristate-12-acetate, phorbol 12-O-tetradecanoylphorbol 13-acetate, phorbol 12, 13 didecanoate, tetradecanoylphorbol acetate, ionomycin, arginine vasopressin, atrial natriuretic peptide, brain natriuretic peptide, tetraethylammonium, colchicine, rhizoxin, estramustine, nocodazole, erbuluzole, and tubulozole.

46. The method of claim 45 wherein the aqueous humor modulating agent is selected from the group consisting of prostaglandin A, prostaglandin B, prostaglandin D, prostaglandin E, prostaglandin F, latanaprost, bimatoprost, unoprostone, travoprost, betaxolol, carteolol, levobunolol, metipranolol, timolol, levobetaxolol, epinephrine, dipivefrin, pilocarpine, pilocarpine hydrochloride, carbachol, demacarium, echothiophate iodine, physostigmine, acetazolamide, methazolamide, dorzolamide hydrochloride ophthalmic solution, dorzolamide hydrochloride-timolol maleate ophthalmic solution, brinzolamide hydrochloride, dorzolamide, and brinzolamide.

47. A method of treating glaucoma in a subject, the method comprising:

- (a) diagnosing a subject in need of treatment for glaucoma; and
- (b) administering to the subject an aquaporin modulating agent and an aqueous humor modulating agent, wherein the aqueous humor modulating agent lowers intraocular pressure by a pathway other than the modulation of aquaporin.

48. The method of claim 47 wherein the glaucoma is selected from the group consisting of primary open angle glaucoma, secondary open angle glaucoma, primary angle closure glaucoma, secondary angle closure glaucoma, congenital glaucoma, and normal pressure glaucoma.

49. The method of claim 47 wherein the aquaporin modulating agent is selected from the group consisting of an angiotensin converting enzyme inhibitor, a protein kinase C activator, a protein kinase A inhibitor, a vasoactive peptide, and a vinca alkaloid.

50. The method of claim 49 wherein the aqueous humor modulating agent is selected from the group consisting of a prostaglandin, a prostaglandin analog, a beta adrenergic antagonist, an adrenergic agonist, a cholinergic agonist and a carbonic anhydrase inhibitor.

51. The method of claim 47 wherein the aquaporin modulating agent is selected from the group consisting of enalapril, benazepril, captopril, fosinopril, lisinopril, moexipril, quinapril, ramipril, trandolapril, phorbol 12, 13 dibutyrate, phorbol 12-myristate-12-acetate, phorbol 12-O-tetradecanoylphorbol 13-acetate, phorbol 12, 13 didecanoate, tetradecanoylphorbol acetate, ionomycin, arginine vasopressin, atrial natriuretic peptide, brain natriuretic peptide, tetraethylammonium, colchicine, rhizoxin, estramustine, nocodazole, erbuluzole, and tubulozole.

52. The method of claim 51 wherein the aqueous humor modulating agent is selected from the group consisting of prostaglandin A, prostaglandin B, prostaglandin D, prostaglandin E, prostaglandin F, latanaprost, bimatoprost, unoprostone, travoprost, betaxolol, carteolol, levobunolol, metipranolol, timolol, levobetaxolol, epinephrine, dipivefrin, pilocarpine, pilocarpine hydrochloride, carbachol, demacarium, echothiophate iodine, physostigmine, acetazolamide, methazolamide, dorzolamide hydrochloride ophthalmic solution, dorzolamide hydrochloride-timolol maleate ophthalmic solution, brinzolamide hydrochloride, dorzolamide, and brinzolamide.

53. The method of claim 1 wherein the subject is a human.

54. The method of claim 1 wherein the aquaporin modulating agent and the aqueous humor modulating agent are administered substantially simultaneously.

55. The method of claim 1 wherein the aquaporin modulating agent and the aqueous humor modulating agent are administered sequentially.